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(57) Abstract

The present invention provides a dosimetric package, a method of making the dosimetric package, and a method of characterizing a dosimetric package. The dosimetric package includes one or more products, one or more packaging materials covering at least a portion of the one or more products, as well as one or more integral dosimetric agents incorporated into the dosimetric package, such that the package itself possesses properties detectable by dosimetric analysis. The dosimetric package of the present invention may be dosimetrically analyzed, the result of which may be utilized to further determine characteristics of the dosimetric package such as, amount of ionizing radiation received by the dosimetric package, relative sterility, relative freshness, and the like.

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DOSIMETRIC PACKAGE AND METHODS OF MAKING AND CHARACTERIZING SAME

BACKGROUND INFORMATION

1. Field of the Invention

The present invention relates generally to a package incorporating an integral dosimetric agent, a method of making the package, and a method of characterizing the package. The integral dosimetric agent has a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis. By incorporating such a dosimetric agent into the package, the package itself possesses dosimetric properties such that the amount of radiation received by the package, either during a certain time period or over the lifetime of the package, may be accurately and easily determined.

2. Background of the Invention

Irradiation is an increasingly important manufacturing step in many industrial applications for a wide variety of purposes. For example, irradiation is used in the medical device/instrument industry to sterilize devices or instruments at several stages of manufacture, including at the point that such devices or instruments are or have been packaged in final form. Irradiation is also becoming widely used in the food and beverage industry to reduce or eliminate bacteria or other undesirable contaminants in food and beverage items. Irradiation also is employed in the manufacture of pharmaceuticals, personal hygiene products, cosmetics, etc., to sterilize such products.

Many of the aforementioned products have rigid manufacturing and/or quality requirements due to their intended end use. Thus, although irradiation is generally an effective sterilization/cleansing technique, it would in many instances be desirable, if not required, to confirm that the products had received the amount of irradiation necessary to achieve the desired purpose. Such confirmation has heretofore been provided via the use of external dosimeters placed in proximity to the products being irradiated. Dosimeters are devices that provide a measurable response that relates, and in some instances is proportional to, the amount of radiation that the dosimeter receives. Thus, by placing these devices in proximity to the product(s) that are being irradiated,

the amount of radiation that has been received by the product can be inferred from the amount of radiation that has been received by the dosimeter.

Although generally an effective means of determining the amount of radiation received by a product, the use of external dosimeters as a measure of radiation received by products in close proximity thereto is inadequate for some applications. Often, one external dosimeter is associated with many different products at the same time. The dosage of radiation received by the dosimeter is assumed to be the same as that received by all the associated products, but this is not always the case. Due to fluctuations in irradiation, differences in distance to the radiation source, differences in radiation absorbance due to difference in product material, and other such properties, the amount of radiation received by the external dosimeter and each individual product may not be equivalent. The uncertainty in the amount of radiation received by each product that is necessarily present as a result of this product-to-product variability is undesirable, if not unacceptable, for many applications. In some industries, manufacturing specifications require a greater degree of confidence than can be provided by mere inference.

Furthermore, external dosimeters are no longer useful to characterize a product once that product has left the point of manufacture and entered a stream of commerce. For example, many products are subjected to irradiation for sterilization purposes in large lots. For many of these products, it may be desirable, if not required, to be able to determine or validate whether the product has been adequately sterilized at a later date. However, relying on external dosimeters at the point of manufacture to determine the amount of radiation received by the product once the product enters a stream of commerce typically requires utilization of extensive recordkeeping to provide a means of later validating the amount of radiation received. If such a later validation becomes necessary, record retrieval is required. Introducing these additional recordkeeping and retrieval steps into the manufacturing process not only is time consuming but also costly and presents opportunity for the introduction of error.

Thus, a need to more accurately measure the amount of radiation that an individual product has received continues to exist. Such accurate measurement can allow a product manufacturer, and/or subsequent user or purchaser, to evaluate whether a product has received an amount of radiation sufficient to achieve a desired purpose,

e.g. relative freshness, sterilization, reduction/elimination in bacteria or other contaminants, and the like.

SUMMARY OF THE INVENTION

The present invention provides a package that incorporates a dosimetric agent as part of the package itself. In this manner, the package acts as its own dosimeter, i.e., it is a dosimetric package. As a result, the dosimetric package can be subjected to dosimetric analysis to determine the amount of radiation that the package has received without relying upon external dosimeters. By utilizing the package itself as a dosimeter, rather than relying on an external dosimeter, uncertainty in the amount of radiation received by an individual package as a result of the aforementioned package-to-package variation is reduced or eliminated. Thus, the dosimetric package of the present invention provides a more accurate measure of the amount of radiation received by the package than typically is provided by an external dosimeter. Furthermore, such a determination may be made after the package has left the point of manufacture and entered a stream of commerce.

In one aspect, the present invention provides a dosimetric package that includes one or more products and one or more packaging materials covering at least a portion of the one or more products, as well as a method of making the dosimetric package. In addition to the product(s) and packaging material(s), the dosimetric package includes one or more integral dosimetric agents, such that the package itself possesses properties detectable by dosimetric analysis. Since preferred methods of dosimetric analysis do not involve the transmission or reflectance of light, the dosimetric agent(s) may preferably and advantageously be incorporated into either or both of the product(s) or packaging material(s) without regard to the ultimate location of the dosimetric agent. Preferred dosimetric agents are those which have a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis. Particularly preferred dosimetric agents are those which have a free radical state as their second, activated state.

A dosimetric package in accordance with the present invention can itself be subjected to dosimetric analysis, so that analyzing the dosimetric package provides a reliable, accurate assessment of the amount of radiation received by the package. The

amount of radiation received may, in turn, be utilized to determine other desired characteristics or properties of the package, including for example, relative freshness, effectiveness of sterilization treatment, and the like.

In another aspect, the present invention provides a method of characterizing a dosimetric package that includes the steps of providing a dosimetric package as just described and subjecting it to dosimetric analysis, preferably spectroscopic analysis. The spectroscopic response is measured and, utilizing a correlation between the characteristic in question and the measured spectroscopic response, the dosimetric package may be characterized. Such a correlation, for example, may be between the amount of ionizing radiation received and the spectroscopic response such that the amount of ionizing radiation that the dosimetric package received is determined. In certain preferred embodiments, the method further includes, prior to subjecting the dosimetric package to dosimetric analysis, the step of subjecting the dosimetric package to a treatment effective to cause at least a portion the integral dosimetric agent to be activated to the second, activated state. Where the second, activated state is a free radical state, the treatment preferably includes exposure to ionizing radiation such as gamma ray, electron beam, corona discharge, plasma discharge, X-rays, microwave energy, combinations of these, and the like.

To assist in understanding the description of the invention that follows, provided immediately below are certain definitions which apply hereinthroughout unless a contrary intention is explicitly indicated:

"free radical" means a molecular fragment having one or more unpaired electrons, wherein the fragment is formed by splitting a covalent bond;

"monomer" means a single, one unit molecule capable of combination with itself, or other monomers, to form oligomers or polymers;

"oligomer" means the polymerization product of 2 to 20 monomers;

"polymer" means the polymerization product of 21 or more monomers and is inclusive of homopolymers, copolymers, and interpolymers as well as blends and modifications thereof;

"mer unit" means that portion of a polymer derived from a single monomer; for example, a mer unit derived from ethylene has the general formula —CH_2CH_2—;

"homopolymer" means a polymer consisting essentially of a single type of repeating mer unit;

"copolymer" means a polymer that includes mer units derived from two monomers and is inclusive of random, block, segmented, graft, etc., copolymers;

"interpolymer" means a polymer that includes mer units derived from at least two monomers and is inclusive of copolymers, terpolymers, tetrapolymers, and the like;

"(meth)acryl" means methacryl, acryl, and homologs thereof in which the substituent on the carbon atom in the alpha position relative to the carboxyl moiety may not only be hydrogen (acryl) or methyl (methacryl), but may also be lower alkyl or cycloalkyl or other suitable monovalent moieties;

"longitudinal direction" means that direction along a film and parallel to the machine direction;

"transverse direction" means that direction across a film and perpendicular to the longitudinal direction;

"free shrink" means the percent dimensional change, as measured by ASTM D 2732, in a 10 cm × 10 cm specimen of film when it is subjected to heat;

as a verb, "laminate" means to affix or adhere (by means of, for example, adhesive bonding, pressure bonding, corona lamination, and the like) two or more separately made film articles to one another so as to form a multilayer structure; as a noun, "laminate" means a product produced by the affixing or adhering as just described;

"directly adhered," as applied to film layers, means adhesion of the subject film layer to the object film layer, without a tie layer, adhesive, or other layer therebetween;

"inner layer" means a layer of a film having each of its principal surfaces directly adhered to one other layer of the film;

"outer layer" means a layer of a film having less than both of its principal surfaces directly adhered to other layers of the film;

"barrier layer" means a film layer capable of excluding one or more gases (e.g., O_2);

"abuse layer" means an outer layer and/or an inner layer that resists abrasion, puncture, and other potential causes of reduction of package integrity and/or appearance quality;

"tie layer" means an inner layer having the primary purpose of providing interlayer adhesion to adjacent layers that include otherwise non-adhering polymers;

"bulk layer" means any layer which has the purpose of increasing the abuse resistance, toughness, modulus, etc., of a multilayer film and generally includes polymers that are inexpensive relative to other polymers in the film which provide some specific purpose unrelated to abuse resistance, modulus, etc.;

"comprising" is an open-ended term that means that the recited elements are only a part of the product, method or system and that the composition, product, method, system, or the like may include other elements not explicitly mentioned; and

"seal layer" (or "sealing layer" or "heat seal layer" or "sealant layer") means

(a) with respect to lap-type seals, one or more outer film layer(s) involved in the sealing of the film to itself (in some circumstances, as much as the outer 75 μm of a film can be involved in the sealing of the film to itself or another layer), another film layer of the same or another film, and/or another article which is not a film, or

(b) with respect to fin-type seals, an inside film layer of a package, as well as supporting layers within 75 μm of the inside surface of the innermost layer, involved in the sealing of the film to itself; and

as a noun, "seal" means a bond of a first region of a film surface to a second region of a film surface (or opposing film surfaces) created by heating (e.g., by means of a heated bar, hot air, infrared radiation, ultrasonic sealing, etc.) the regions (or surfaces) to at least their respective softening points so as to cause bonding between polymer chains.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The following embodiments of the present invention are not intended to be exhaustive or to limit the invention to the precise forms disclosed in the following detailed description. Rather the embodiments are chosen and described so that others

skilled in the art may appreciate and understand the principles and practices of the present invention.

The present invention provides a package, a method of making a package, and a method of characterizing a package, wherein the package includes at least one dosimetric agent that is part of the package itself. Because the integral dosimetric agent is incorporated into either one or both of the product or packaging material of the package of the present invention, the package itself acts as a dosimeter, i.e., incorporating a dosimetric agent into a component of the package results in a package with dosimetric properties. As a result, a dosimetric package in accordance with the present invention can itself be subjected to dosimetric analysis to determine the amount of irradiation that the dosimetric package has received.

By relying on the dosimetric package itself, rather than an external dosimeter, a more accurate assessment of the amount of radiation received by the package and/or the packaged product may be made. External dosimeters may accurately provide dosimetric information as to the dosimeter itself, but can only provide approximate dosimetric information about items in proximity to the external dosimeter. In typical industrial applications where several items are irradiated simultaneously or serially, the amount of radiation received by each individual item is not necessarily uniform. Thus, the use of an external dosimeter may not provide optimal dosimetric accuracy in these circumstances. In contrast, the dosimetric package of the present invention provides a very accurate measure of the dosage of radiation it has received, regardless of package-to-package variation in the amount of radiation received.

Once the amount of radiation received by the dosimetric package has been accurately determined, this information then can be utilized in a wide variety of applications to determine other desired characteristics or properties of the dosimetric package, including relative freshness, effectiveness of sterilization treatment, and the like. For example, the method and package of the present invention are particularly useful in the medical field, where they provide the ability to verify that dosimetric packages including medical instruments or devices have received sufficient amounts of radiation to effectively sterilize the device or instrument to the desired degree. The dosimetric package and methods in accordance with the present invention also find particular utility in the food and beverage industry, where irradiation is used to

eliminate bacteria or other undesirable contaminants in packaged food and beverage items. In this application, the method and package of the present invention allow the amount of radiation that a food or beverage item has received to be verified to ensure the shelf life and freshness of the food or beverage item. In these, as well as many other applications, the method and package of the present invention may be used not only as a quality control mechanism at the point of manufacture, but also as a means to verify the amount of radiation received by a product at any point within the stream of commerce.

Regardless of the application, a manufacturer, packager, retailer, consumer, etc., may have a desire to determine or confirm whether a manufactured or purchased item has been exposed to a sufficient amount of radiation to achieve the desired purpose. The methods and dosimetric package of the present invention provide an easy manner by which to obtain the desired determination or confirmation. By simply subjecting a dosimetric package in accordance with the present invention to dosimetric analysis, the amount of radiation received by the dosimetric package can be easily determined/confirmed.

Dosimetric packages in accordance with the present invention generally include one or more products and one or more packaging materials covering at least a surface portion of the one or more products, wherein at least one dosimetric agent is incorporated into the dosimetric package to provide dosimetric capabilities. Any type of dosimetric agent, or combination of such agents, may be incorporated into the dosimetric package of the present invention, although some dosimetric agents may be more suitable for some applications than others. Selecting a suitable dosimetric agent(s) depends on many factors including the type of product or packaging material into which the dosimetric agent(s) will be incorporated, the dosage of radiation to be received by the dosimetric package, the amount of time between irradiation and spectroscopic analysis, and the like.

Advantageously, dosimetric agents generally retain their dosimetric characteristics even when mixed, blended, compounded, or otherwise physically combined with almost all materials, whether solid or liquid. Thus, so long as the material(s) and the dosimetric agent(s) do not react with each other in a manner that degrades or destroys the dosimetric characteristics of the agent(s), and so long as the act of combining the material(s) and agent(s) does not involve processing conditions that

affect the dosimetric characteristics of the agent(s), the dosimetric agent(s) may be incorporated into virtually any material chosen for use in the product or the packaging material of the dosimetric package of the present invention. Examples of materials that may be advantageously used in the dosimetric packages of the present invention include heterogeneous or homogeneous blends, mixtures, solutions, composites, and the like, of organic or inorganic substances such as monomers, oligomers, polymers, ceramic materials, wood, metals (including pure metals, metal alloys, intermetallic compositions, and the like), paperboard, chipboard, cardboard and the like. Clearly, the choice of dosimetric agent is not particularly limited by the materials of the product or packaging material of the present invention.

Preferred dosimetric agents for use in the methods and dosimetric package of the present invention include substances that have a first, latent state that provides a first spectral response to spectroscopic analysis and a second, activated state that provides a second, distinguishable spectral response to spectroscopic analysis. Particularly preferred substances to be used as a dosimetric agents are those that are "truly latent", i.e., those that have a first, latent state which provides no more than a negligible response to spectroscopic analysis and thus, are typically detectable only upon activation. As a result, dosimetric packages incorporating truly latent dosimetric agents that are in their latent state can provide the same response to spectroscopic analysis as a package that does not include an amount of the dosimetric agent. The use of truly latent substances as dosimetric agents can thus reduce the amount of error in subsequent dosimetric measurements.

Particularly preferred dosimetric agents include substances for which the second, activated state is a free radical state. Such a state is achievable, for example, by irradiating the dosimetric agent with ionizing radiation such as gamma radiation, electron beam radiation, corona discharge, plasma discharge, X-rays, microwave energy, combinations of these, and the like. When so irradiated, dosimetric agents in accordance with this embodiment of the present invention form free radicals in amounts corresponding to the dosage of radiation. The resultant free radicals then can be spectroscopically analyzed. The strength of the resultant spectroscopic signal can correspond to the amount of free radicals in, and hence the dosage of radiation received by, the dosimetric package.

Using dosimetric agents that have a free radical state as a second, activated state is particularly advantageous, because electron spin resonance spectroscopy (ESRS), also known as electron paramagnetic resonance spectroscopy, can be used as a detection method. ESRS is a spectroscopic technique used to detect free radicals which does not rely upon light absorption or reflection to detect free radicals or to generate a spectroscopic response. As a result, dosimetric agents can be incorporated into any material, and thus any desired portion, of the dosimetric package without consideration of the optical transparency or transmission capabilities of that portion of the dosimetric package. Furthermore, such dosimetric agents may be incorporated into, or on the surface of, an outer layer of packaging material, or may be incorporated into an inner layer of the product to be packaged without affecting the detectability of the free radical response.

Examples of integral dosimetric agents that have a free radical state as a second, activated state include, but are not limited to, amino acids, such as alanine and glutamine; sugars, such as sucrose, lactose, glucose, mannose, maltose, and the like; amine salts (such as methyl amine salts, dimethyl amine salts, trimethyl amine salts and the like) of organic acids, for example, amine salts of oxalic acid, malonic acid, succinic acid or glutaric acid; combinations of the foregoing; and the like. Amino acids represent a preferred class of integral dosimetric agents because free radicals of amino acids are relatively stable, are biocompatible, are easily detected by ESRS, are readily available at economic prices, and/or are readily purified.

The integral dosimetric agent used in the methods and/or dosimetric package of the present invention preferably include one or more isomers of alanine. Alanine is an amino acid having the formula $CH_3C(NH_2)HCOOH$ in the ground state and forms a free radical (believed to be CH_3-CH*-COOH) when exposed to ionizing radiation. The term "alanine" is meant to contemplate all of the various structural and isomeric forms of alanine, such as α-alanine, its optical isomers D-alanine, and L-alanine, DL-alanine, the linear isomer of alanine, β-alanine and combinations of these. Alanine is a particularly preferred integral dosimetric agent for several reasons. First, incorporation of dosimetric amounts of alanine into typical polymeric packaging materials does not generally substantially alter the mechanical or rheological properties of the polymer(s) used to form the package. Second, isomers of alanine form very stable free radicals. In

the case of L-alanine, the half life has been estimated to be as long as 50 years. Furthermore, alanine is generally considered to be biocompatible, being one of the building blocks of DNA and present in the human bloodstream. As a result, its use in food contact applications such as food/beverage packaging is likely to have already received FDA approval or is suitable for FDA approval.

Advantageously, the first, latent state of alanine is also truly latent with respect to ESRS. That is, the latent state of alanine provides a negligible ESR signal, if any at all. Yet, after irradiation, alanine is converted to a free radical that provides a very strong ESR signal. As still another advantage, alanine has a relatively high degradation temperature, e.g., about 300°C, allowing it to be incorporated in products or packaging materials whose manufacture involves temperatures up to about 295°C.

The dosimetric agent(s) may be incorporated in one or more products of the dosimetric package, in one or more packaging materials of the dosimetric package, or in both of the one or more products and one or more packaging materials. When incorporated in a product or packaging material, the dosimetric agent can be incorporated in one or more locations so that multiple parts of the dosimetric package are detectable by dosimetric techniques. Most preferably, at least one dosimetric agent is incorporated in a packaging material such that the packaging material itself acts as a dosimetric agent.

Preferred packaging materials for use in the dosimetric package of the present invention are flexible thermoplastic and/or thermosetting films. Such films advantageously are easily conformed substantially to a wide variety of different shapes and surfaces to be packaged. Additionally, many such films are optically transparent, thus allowing potential customers to view the packaged product. Such films can be made by a variety of manufacturing techniques known to the ordinarily skilled artisan including one or more of laminating, blowing, casting, extruding, pressing, molding, coextruding, and the like.

For certain applications, a coextruded, multilayer packaging film which has been oriented, most preferably biaxially oriented, may be preferred. Orienting involves initially cooling an extruded film to a solid state (by, for example, chilled water, air, or other fluid) followed by reheating the film to a temperature within its orientation temperature range and subsequently stretching the film. The stretching step can be

accomplished in many ways, such as for example, by blown bubble or tenter framing techniques, both of which are known to those of ordinary skill in the art. After being heated and stretched, the film is quenched rapidly while being maintained in its stretched configuration so as to lock in the oriented molecular configuration. This combination of elongation at elevated temperature followed by cooling causes an alignment of the polymer chains to a more parallel configuration, thereby dramatically altering the mechanical properties of the film. When an unrestrained, unannealed, oriented film subsequently is heated to (or near) its orientation temperature, the film shrinks almost to its original, i.e., pre-elongation, dimensions. Such a film is said to be heat shrinkable. For certain end use applications, a film for use as the packaging material in the process of the present invention preferably can be both biaxially oriented and heat shrinkable.

Oriented films typically are oriented in several directions, usually two directions perpendicular to one another. Orientation in the longitudinal (L) direction is referred to as drawing, whereas orientation in the transverse (T) direction is referred to as stretching. For films extruded through an annular die, stretching occurs when the film is blown to produce a bubble. Thereafter, drawing occurs when the film passes through two sets of powered nip rolls, with the downstream set having a higher surface speed than the upstream set. The resulting draw ratio is the surface speed of the downstream set of nip rolls divided by the surface speed of the upstream set of nip rolls.

Oriented films for use in the methods and/or dosimetric package of the present invention preferably have a shrink tension of at least about 700 kPa, more preferably at least about 1050 kPa, and most preferably at least about 1400 kPa. Additionally, they can exhibit a Young's modulus (measured in accordance with ASTM D 882) of at least about 100 MPa up to about 1750 MPa.

Oriented films generally have an L direction free shrink of at least about 1% and a T direction free shrink of at least about 1% (both measured at 85°C). Where desirable for a particular application, an oriented film can have a free shrink (at 85°C) in at least one of the L and T directions of at least 2%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, even up to 50%. A film can be biaxially oriented and have a free shrink (at 85°C) in each of the L and T directions of from about 1% to about 20%, more preferably from about 2% to about 15%, and even more preferably from about 3% to

about 10%, and a total free shrink (L + T) of from about 2% to about 40%, preferably from about 2.5% to about 30%, more preferably from about 3% to about 20%, and still more preferably from about 5% to about 15%. For certain applications, orienting followed by heat setting or annealing a film so as to provide a T direction free shrink (at 85°C) of less than 10%, more preferably less than 5%, can be preferred. Heat setting can be accomplished at a temperature from about 60°C to about 200°C, preferably from about 70°C to about 150°C, and more preferably from about 80°C to 90°C.

Where a film for use in the methods and/or dosimetric packages of the present invention is shrinkable, it preferably includes up to about 20 layers, more preferably from about 3 layers to about 12 layers (especially where the total number of layers is an odd number), although any number of layers are feasible as long as the film provides the desired properties for the particular packaging operation in which it is to be used. Regardless of the particular number or order of the film layers, those films with at least one layer that includes a polymer including mer units derived from ethylene are useful for many end use applications.

A film used as the packaging material in the methods or dosimetric packages of the present invention optionally can be subjected to an energetic radiation treatment produced by, for example, corona discharge, plasma, flame, ultraviolet, X-ray, γ-ray, β-ray, or high energy electron systems so as to induce crosslinking between polymer chains. Such irradiative crosslinking of polymeric films is disclosed in, for example, U.S. Patent No. 4,064,296 (Bornstein et al.), the teaching of which is incorporated herein by reference. Suitable levels of radiation range from about 2 MR to about 15 MR, preferably from about 2 MR to about 10 MR. The desired dosage of radiation can depend on the film composition, thickness, etc., as well as the desired end use of the film. A film used in the dosimetric package and/or methods of the present invention can be used as, or in connection with irradiated, oriented, heat set films and/or can be laminated, adhesively adhered, extrusion coated, or extrusion laminated onto a substrate to form a laminate. If such a such an irradiatively crosslinked film is to be included in the dosimetric package of the present invention, and furthermore, if a dosimetric agent that has a free radical state as its second, activated state, is to be included in the irradiatively crosslinked film, the crosslinking radiation applied can have the effect of

activating at least a portion of the dosimetric agent into its second, activated state. As is understood by one of ordinary skill in the art of dosimetry, the effect is simply cumulative and can be readily translated to yield the amount of subsequent radiation received by the article or package.

Films used in the packaging industry can be categorized according to the number of component layers. Some films are made from a single polymer or blend of polymers and thus have only one layer. However, most commercially available packaging films include more than one layer, i.e., are multilayer films. In general, the layers of a multilayer film can be classified as inner or outer. Additionally, any number of tie layers can be included. The number of layers present in a film used as a packaging material in the methods or dosimetric package of the present invention is unimportant. Rather, if the dosimetric agent is to be incorporated into the film, it can be incorporated into any one of the multiple layers, as the location of the dosimetric agent within the package is not critical inasmuch as the dosimetric agent may be activated and detected from any position in or on the dosimetric package.

When the packaging material used in the methods and/or dosimetric package of the present invention is a multilayer film, it can include those films that have one or more of the following types of layers: abuse layers, barrier layers, tie layers, bulk layers, and seal layers. The physical properties required of a film for any given end use application often determine the composition of the film and/or the compositions of the various layers of the film. Where a variety of properties are required, a variety of layers containing differing polymeric components can be, and usually are, employed.

For example, if the product(s) being packaged is/are desirably protected from one or more detrimental materials (e.g., atmospheric O_2), a barrier layer including, for example, ethylene/vinyl alcohol interpolymer (EVOH), vinylidene chloride interpolymer, or one or more of certain polyamides (e.g., nylons) can be included in the multilayer film structure. If the barrier layer employed is one comprising a material known to be sensitive to moisture, such as EVOH, and the application requires exposure of the film to moisture, then one or more moisture barrier layers also can be included. If the film is likely to be subjected to abuse during handling and/or transport, an abuse layer can be provided (either as an inner or outer layer). One or two seal layers can be provided to allow for sealing of the film to itself or another packaging material during the formation of a

dosimetric package. One or more inner layers also can be provided, and films with at least one inner layer are preferred for many applications.

Where a flexible film to be used in the methods and/or dosimetric package of the present invention is a multilayer film, those films containing at least one layer including a polymer that includes mer units derived from ethylene can be preferred for some end use applications. These polymers can be ethylene homopolymers or they also can include mer units derived from one or more of (meth)acrylic acid, a C_3-C_{20} α-olefin, C_1-C_{20} esters of (meth)acrylic acid, vinyl acetate, and vinyl alcohol. Ionomers also can be useful. Particularly preferred for many applications are ethylene/α-olefin interpolymers.

The relatively recent advent of single site-type catalysts (e.g., metallocenes) necessitates further definitional clarification when discussing ethylene homo- and copolymers. Heterogeneous polymers are those having relatively wide variation in molecular weight and composition distribution. Polymers prepared with, for example, conventional Ziegler Natta catalysts are heterogeneous. Such polymers can be used in a variety of layers including the seal layer(s). On the other hand, homogeneous polymers have relatively narrow molecular weight and composition distribution. Homogeneous polymers differ structurally from heterogeneous polymers in that they exhibit a relatively even sequencing of comonomers within a chain, a mirroring of sequence distribution in all chains, and a similarity of chain lengths, i.e., a narrower molecular weight distribution. Homogeneous polymers typically are prepared using metallocene or other single site-type catalysts. Homogeneous polymers also can be used in a variety of layers including the seal layer(s).

The term "ethylene/α-olefin copolymer" (or interpolymer) as used herein refers both to heterogeneous materials such as low density polyethylene (LDPE), medium density polyethylene (MDPE), linear low density polyethylene (LLDPE), and very low and ultra low density polyethylene (VLDPE and ULDPE), as well as to homogeneous materials which, in general, are prepared by the copolymerization of ethylene and one or more α-olefins. The comonomer preferably is a C_4-C_{20} α-olefin, more preferably a C_4-C_{12} α-olefin, still more preferably a C_4-C_8 α-olefin. Particularly preferred α-olefins include 1-butene, 1-hexene, 1-octene, and mixtures thereof. In general, from about 80 weight percent to about 99 weight percent ethylene and from about 1 weight percent to

about 20 weight percent α-olefin, preferably from about 85 weight percent to about 95 weight percent ethylene and from about 5 weight percent to about 15 weight percent α-olefin, a copolymerized in the presence of a single site catalyst. Examples of commercially available homogeneous materials include the metallocene catalyzed Exact™ resins (Exxon Chemical Co.; Baytown, Texas), substantially linear Affinity™ and Engage™ resins (Dow Chemical Co.; Midland, Michigan), and Tafmer™ linear resins (Mitsui Petrochemical Corp.; Tokyo, Japan).

Homogeneous ethylene/α-olefin copolymers can be characterized by one or more methods known to those of skill in the art, such as molecular weight distribution (M_w/M_n), composition distribution breadth index (CDBI), narrow melting point range, and single melt point behavior. Molecular weight distribution, also known as polydispersity, can be determined by, for example, gel permeation chromatography. Homogeneous ethylene/α-olefin copolymers to be used in a layer of the film of the present invention preferably have an M_w/M_n of less than 2.7; more preferably from about 1.9 to about 2.5; still more preferably, from about 1.9 to about 2.3.

The CDBI of homogeneous ethylene/α-olefin copolymers generally is greater than about 70%. CDBI is defined as the weight percent of copolymer molecules having a comonomer content within 50%, i.e., ± 50% of the median total molar comonomer content. CDBI can be determined by temperature rising elution fractionation as described by, for example, Wild et al., *J. Poly. Sci. - Poly. Phys. Ed.*, vol. 20, 441 (1982). Linear polyethylene, which does not contain a comonomer, is defined to have a CDBI of 100%. CDBI determination clearly distinguishes homogeneous copolymers (CDBI values generally above 70%) from presently available VLDPEs (CDBI values generally less than 55%).

Homogeneous ethylene/α-olefin copolymers also typically exhibit an essentially single melting point with a peak melting point (T_m), as determined by differential scanning calorimetry (DSC), of from about 60°C to about 105°C, more precisely a peak T_m of from about 80° C to about 100°C. As used herein, the phrase "essentially single melting point" means that at least about 80% (by weight) of the material corresponds to a single T_m at a temperature within the range of from about 60°C to about 105°C, and essentially no substantial fraction of the material has a peak melting point in excess of

about 115°C as determined by DSC analysis (e.g., on a Perkin Elmer™ System 7 Thermal Analysis System). The presence of higher melting peaks has been found to be detrimental to film properties such as haze and seal initiation temperature.

Of course, additives commonly included in thermoplastic or thermosetting films also can be included in a film used in the methods or dosimetric package of the present invention. Typical additives include antislip agents, antiblocking agents (particularly diatomaceous earth and alkali aluminosilicate ceramic microspheres), antifogging agents, reinforcements, fillers, extenders, pigments, lubricants, antioxidants, heat stabilizers and the like.

Where the packaging material to be used in the dosimetric package of the present invention is a flexible film, it can take the form of a stretch film, a film suitable for vertical or horizontal form-fill-and-seal end use, a lidstock film, a film suitable for vacuum skin packaging, a film suitable for use as a barrier bag, a film suitable for use as a patch bag, a film suitable for use in case ready packaging, a film suitable for use in a thermoformed container (particularly in a film used as a liner in a thermoformed tray, such as a polystyrene tray), an aroma/odor barrier film, a film suitable for use in cook-in end use applications (especially heat shrinkable bags, heat shrinkable and non-heat shrinkable casings, and containers thermoformed from non-heat shrinkable films and sheets), and/or a medical film. Some specific examples of such flexible films include:

(a) films used to produce bags such as those described in, for example, U.S. Patent Nos. 3,741,253 (Brax et al.), 3,891,008 (D'Entremont), 4,048,428 (Baird), and 4,284,458 (Schirmer);

(b) films used to produce bags for cook-in applications, such as those described in, for example, U.S. Patent Nos. 4,064,296 (Bornstein et al.) and 4,855,183 (Oberle);

(c) films used in connection with patch bags, such as those described in, for example, U.S. Patent No. 4,755,403 (Ferguson);

(d) shrink films such as those described in, for example, U.S. Patent Nos. 4,551,380 and 4,643,943 (both to Schoenberg);

(e) films having oxygen, moisture, or odor barrier functionality such as those described in, for example, U.S. Patent Nos. 4,064,296 (Bornstein et al.), 4,724,185 (Shah), 4,839,235 (Shah), and 5,004,647 (Shah);

(f) films suitable for medical applications such as, for example, those described in U.S. Patent No. 5,695,840 (both to Mueller);

(g) films suitable for use in a thermoformed package such as, for example, those disclosed in U.S. Patent No. 4,735,855 (Wofford et al.);

(h) stretch/shrink-type films such as those disclosed in, for example, U.S. Patent No. 4,617,241 (Mueller);

(i) films suitable for the packaging of flowable or pumpable products such as those disclosed in, for example, U.S. Patent No. 4,746,562 (Fant);

(j) films suitable for packaging, water cooking, and storing food products such as are disclosed in, for example, U.S. Patent Nos. 4,104,404 (Bieler et al.);

(k) hot blown films of a type useful in chub packaging such as are described in, for example, U.S. Patent No. 4,937,112 (Schirmer);

(l) films having LLDPE or LMDPE in a core and/or an intermediate layer, such as those described in, for example, U.S. Patent Nos. 4,532,189 (Mueller) 4,194,039 (Mueller), 4,390,385 (Ferguson et al.), 4,274,900 (Mueller et al.), 4,188,443 (Mueller et al.), and 5,298,302 (Boice);

(m) films having a low shrink energy such as those disclosed in, for example, U.S. Patent Nos. 4,833,024 (Mueller) and 5,023,143 (Nelson);

(n) films suitable for use in vacuum skin packaging applications, such as those disclosed in, for example, U.S. Patent Nos. 4,886,690 (Davis et al.), 4,963,427 (Botto et al.), and 5,075,143 (Bekele);

(o) films including one or more layers that contain a homogeneous polymer such as those disclosed in, for example, European Publication No. 0 597 502 A3 (Babrowicz et al.) as well as U.S. Patent Nos. 5,604,043 (Ahlgren) and 5,491,019 (Kuo); and

(p) films having high oxygen transmission rates such as, for example, those described in U.S. Patent Nos. 5,491,019 (Kuo) and 5,523,136 (Fischer et al.) as well as U.S. Patent Application No. 08/889,000 (Mossbrook et al.).

The teachings of each of the foregoing references are incorporated herein by reference. Those of ordinary skill in the art can envision other types of films and/or other materials which would be useful as the packaging material in the methods and/or dosimetric package of the present invention; these too are within the scope of the present invention.

The manner in which the integral dosimetric agent(s) is/are incorporated into the packaging material is not critical and, thus, can vary extensively. For example, where the packaging material is paperboard, standard blending, printing, and/or overcoating techniques can be used. Where the packaging material is a flexible polymeric film, blending with a polymer melt or solids mixing of the dosimetric agent with a polymeric powder are preferred incorporation techniques, although printing and/or overcoating techniques also can be used. Those of ordinary skill in the art are familiar with these and other similar or substantially identical techniques.

In certain embodiments of the present invention, the integral dosimetric agent may desirably be incorporated into the product. The manner of incorporation of the dosimetric agent into the desired product is not critical, and thus, may be accomplished in a wide variety of ways. As above, the dosimetric agent may be incorporated into the product by overcoating, blending, printing and the like. Furthermore, the identity of the product to be packaged is relatively unimportant. Any product for which it would be desirable to be able to determine whether, or confirm that, a sufficient amount of radiation had been received to achieve the desired purpose can benefit from being incorporated into the dosimetric package of the present invention, or from being characterized by the method of the present invention. Examples include, but are not limited to, medical devices or instruments, food products, cosmetics, personal hygiene products, pharmaceutical products, and the like.

Some crystalline or other solid substances suitable for use as integral dosimetric agents in the methods or dosimetric package of the present invention tend to yield more isotropic ESRS signals when utilized as relatively smaller particles. Thus, if such a substance is chosen for use as the dosimetric agent, the dosimetric agent preferably is ground into particles of a size which is as fine as possible prior to incorporation into the package. For example, if alanine is to be utilized as the integral dosimetric agent, the alanine particles are preferably ground to a diameter of about 10 μm or less, more preferably about 5 μm or less, prior to incorporation into the product(s) and/or packaging material(s) of a dosimetric package. Particle diameter can be determined by, for example, a MasterSizer™ light scattering instrument (Malvern Instruments; United Kingdom).

Any conventional grinding or milling technique may be used to reduce the diameter of the dosimetric agent particles. Preferably, the size of the dosimetric agent particles is reduced by jet milling. Jet milling with a Microjet™ Fluid Energy mill (Aljet Division, Fluid Energy Processing and Equipment Co.; Plumsteadville, PA), for example, has provided ground alanine with a particle size of about 5 μm.

The dosimetric agent may be incorporated into a product and/or packaging material in any amount effective to provide a detectable spectroscopic response. The amount of dosimetric agent relative to the amount of the material of the product or packaging material preferably is not so high that the final product or packaging material does not possess the necessary properties to be useful in the desired practical application of the product or packaging material. However, the dosimetric package of the present invention desirably contains enough of the dosimetric agent relative to the product or packaging material so as to provide dosimetric capabilities. As general guidelines, bearing these considerations in mind, the dosimetric agent may be incorporated into the product or packaging material in amounts of from about 0.001 ppm to about 95 weight percent of dosimetric agent relative to the total weight of the product or packaging material. As one specific example, when the dosimetric agent includes alanine and is to be incorporated into a polymeric packaging material, using from about 10 ppm to about 30 weight percent, preferably from about 50 ppm to about 10 weight percent, more preferably from about 100 ppm to about 5 weight percent, has been found to be suitable.

As one specific example of an approach for preparing a dosimetric package in accordance with the present invention wherein the dosimetric agent is incorporated into a flexible film packaging material by a blending technique, the dosimetric agent and the material(s) selected for use as the packaging material first can be admixed until a substantially homogeneous mixture results. Such mixing can take place at room temperature or at an elevated temperature depending on the nature of the selected materials. Furthermore, the dosimetric agent and material(s) may be mixed together manually or by mechanical means, such as by a roll mill. Once a substantially homogeneous mixture has been formed, the mixture can be extruded, flow coated, pressed, blow molded, or otherwise processed to form a packaging film or layer of such a film of the desired dimensions and structure.

The particular parameters of each fabrication technique can depend on the particular packaging material and dosimetric agent chosen. More specifically, the parameters chosen should be effective to allow formation of a film or film layer of the desired dimensions, while not adversely affecting the dosimetric properties of the dosimetric agent(s).

Once such a packaging material and/or product incorporating an integral dosimetric agent in accordance with the present invention has been produced, a dosimetric package of the present invention can be formed simply by wrapping or enclosing the product in at least the packaging material, the mechanics of which depend on the nature of the packaging material and of the product. Such packaging may occur, for example, by placing a product in a paperboard container that has been coated with an integral dosimetric agent; a product incorporating a dosimetric agent may be placed in such a paperboard container; a product may be placed into a paperboard container, which container is subsequently shrink wrapped in a packaging film comprising an integral dosimetric agent; and the like.

A dosimetric package in accordance with the present invention may be characterized easily and advantageously by subjecting the dosimetric package to dosimetric analysis to determine the amount of dosimetric agent which is in or has been converted to, the second, activated state. In certain preferred embodiments, the dosimetric package may, prior to dosimetric analysis, be exposed to an amount of ionizing radiation effective to carry out a desired treatment. This irradiation also can serve to activate at least a portion of the integral dosimetric agent incorporated therein to the second, activated state of the dosimetric agent. For example, where the second, activated state of the dosimetric agent is a free radical state, radiation in the form of gamma radiation, electron beam radiation, corona discharge, plasma discharge, X-rays, microwave energy, combinations of these, and the like, can be sufficient to activate at least a portion of the dosimetric agent to the free radical state. The amount of free radicals formed corresponds to the amount of radiation received by the package.

The particular type of dosimetric analysis used to characterize the dosimetric package depends on the nature of the dosimetric agent incorporated into the dosimetric package. For dosimetric agents that form free radicals when irradiated, spectroscopy capable of detecting free radicals is most preferably used. An example of such

spectroscopy includes ESRS. ESRS is based upon the absorption of microwave radiation by a paramagnetic substance such as a free radical when the paramagnetic substance is placed in a microwave field and is also exposed to a strong magnetic field. The principles, techniques, and applications of ESRS are widely known and are described, for example, in Alger, *Electron Paramagnetic Resonance: Techniques and Applications* (InterScience, NY, 1968); Ayscough, *Electron Spin Resonance in Chemistry* (Methuen & Co. Ltd. London 1967) and Box, *Radiation Effects. ESR and ENDOR Analysis*, (Academic Press, London New York 1977), the disclosures of which are incorporated by reference herein.

In a typical ESRS system, the source of microwave radiation is a klystron tube. A klystron tube is an electronic oscillator in which a beam of electrons is pulsed between a cathode and a reflector. The klystron tube is typically operated to produce monochromatic radiation having a frequency of about 9500 MHz, the approximate resonance frequency for an unpaired electron. The oscillating output of the klystron tube is transmitted to a waveguide by a loop of wire, which sets up a fluctuating magnetic field (electromagnetic radiation) in the guide. The waveguide, which is commonly a rectangular metal tube, transmits the microwave radiation to the sample, which is generally held in a small quartz tube positioned between the poles of a permanent magnet.

Typical settings of an ESR spectrometer include a Klystron frequency of 9.1×10^9 Hz, a magnetic field setting of 3240 G or 324 mT, and a field scan range of 20 mT. RF field modulation amplitude, amplification, microwave power, and time constant are adjusted according to the radiation absorbed dose range. For a dose range of 1 kGy/h, for example, suitable settings include a microwave power setting of 4 mW and a field modulation of 100 kHz at 1 mT. Measurements are typically taken at room temperature. The resulting ESR spectra is typically recorded in derivative form to enhance sensitivity and resolution. The resulting spectra may be analyzed by comparison to spectra obtained from reference dosimetric packages. This comparison may be done either manually or with the aid of a computer.

Many characteristics of a dosimetric package in accordance with the present invention may be determined simply by providing a correlation between the amount of radiation received and the desired characteristic. For example, in that embodiment of

the invention wherein the second activated state of the dosimetric agent is a free radical, a correlation may be provided relating the amount of free radicals produced upon exposure to a known dose of radiation, to the effect of that dosage of irradiation on, e.g., sterility, bacterial load, relative freshness, and the like, in a dosimetric package. Such correlations, if not readily available in the literature, may be simply prepared by one of ordinary skill in the art by preparing dosimetric package standards incorporating known amounts of dosimetric agents and for which a desired characteristic is desired to be altered or imparted. The dosimetric package standards then can be irradiated with a known dosage of radiation and subsequently evaluated to determine the dosimetric response and effect of the irradiation on the desired characteristic. Once such a correlation is provided, it may be utilized to evaluate the spectral response of dosimetric packages in accordance with the present invention, thus determining the desired characteristic of the dosimetric package.

The present invention will now be further described with reference to the following illustrative examples of representative aspects of the present invention.

EXAMPLES

Example 1

Commercially available L-alanine powder was ground to a mean particle size of approximately 5 μm using a Microjet™ Fluid Energy mill and 5 parts by weight of the milled L-alanine was added to 95 parts by weight of Poly-Eth™ 1017 LDPE resin (Chevron Corp.; San Francisco, CA) The blend was extruded and blown into a monolayer film using a ZSK-30 extruder (Krupp Werner & Pfleiderer; Ramsey, NJ).

Portions of this packaging film were separately irradiated at various doses using γ radiation from a cobalt source. The irradiations were performed at the National Institute of Standards and Technology (NIST, Gaithersburg, MD) in a GammaCell 232 cobalt source (MDS Nordion; Toronto) at a dose rate of 9.3 kGy/hr. The temperature during irradiation was 23°C. Eight irradiations to doses ranging from 1 kGy to 150 kGy were performed on the packaging film samples.

The irradiated films then were analyzed via ESRS on a model ECS106 ESR spectrometer equipped with a TMH Cavity (Bruker Instruments Inc.; Billerica, MA). Conditions for the ESRS analysis included a modulation amplitude of 16 G, a

conversion time of 40.96 ms, a time constant of 2.6 s, a sweep time of 42 s, a sweep width of 18 G and at a microwave power of 10 mW. For each sample, the presence of the alanine free radical was detected, and the intensity of the free radical signal was measured. A plot was made correlating ESRS signal intensity to irradiation dose and the resulting data analyzed in an effort to establish a correlation curve between the signal intensity and the irradiation dose that each packaging film experienced.

The data were fit using an equation known to be applicable for dosimetry applications, $y = a/[1 + (x/b)c]$, sometimes referred to as the "Logistic Dose Response" equation. In this equation y is the detected ESRS signal intensity, x is the irradiation dose and a, b and c are constants. Using this algorithm, a correlation coefficient of 0.999 was found, revealing an exceptionally high degree of confidence in the ability of the package to yield accurate dosimetry data for the contents packaged therein.

Example 2

Commercially available L-alanine powder was ground to a mean particle size of roughly 5 μm, added to LDPE resin, and blown into a monolayer film as in Example 1.

Portions of this packaging film were then separately irradiated using a high energy electron beam source under controlled conditions of amperage and exposure time in order to deliver a series of doses. These conditions had previously been calibrated against standards in collaboration with the NIST. Six irradiations at doses ranging from 10 to 170 kGy were performed on the packaging films.

The irradiated films were then analyzed via ESRS as in Example 1. The presence of the alanine free radical was detected and the intensity of the free radical signal was measured. A plot was made comparing ESRS signal intensity to irradiation dose, as described in Example 1, yielding an excellent correlation and revealing a high degree of confidence in the ability of the package to yield accurate dosimetry data for the contents packaged therein.

Example 3

Affinity™ PF1140 homogeneous polyethylene resin (Dow Chemical Co.; Midland, MI) was blended with L-alanine to form a masterbatch resin. Prior to blending, commercially available L-alanine powder was ground to a mean particle size

of roughly 5 μm as in Example 1. Sufficient alanine was added to the masterbatch blend so that the total concentration of alanine in the final coextruded film, described below, was nominally 1000 ppm.

This masterbatch blend was coextruded with a variety of other commercially available resins to form a 9-layer film. These resins included Affinity™ PL1850 polyethylene resin (Dow Chemical Co.), Escorene™ PD-9302 ethylene/propylene copolymer containing 3% ethylene (Exxon Chemical Co.), Eval™ LC E151A ethylene/vinyl alcohol copolymer containing 44% vinyl alcohol (Evalca, Pasadena, TX), Elvax™ 3165 ethylene/vinyl acetate copolymer containing 18% vinyl acetate (E.I. Dupont de Nemours & Co.; Wilmington, DE), Surlyn™ 1601, ionomer resin (Dupont), Fortiflex™ J60-500 high density polyethylene (Solvay Advanced Polymers, Inc., Houston, TX), Bynel™ E302 anhydride grafted polypropylene (Dupont), and Bynel™ CXA 3062 anhydride grafted ethylene/vinyl acetate copolymer containing 16% vinyl acetate (Dupont).

The resins were coextruded in a manner such that the alanine containing masterbatch blend formed an inner layer and accounted for approximately 35% of the total film weight. The final film thickness was 6.6×10^3 μm.

Portions of the nine-layer packaging film were separately irradiated using a high energy electron beam source under controlled conditions of amperage and exposure time to deliver a series of doses. These conditions had previously been calibrated against standards in collaboration with (NIST). Eleven irradiations to doses ranging from 100 to 240 kGy were performed on the packaging films.

The irradiated films were analyzed via ESRS as in Example 1. The presence of the alanine free radical was detected, and the intensity of the free radical signal was measured. A plot was made comparing ESR signal intensity to irradiation dose, as described in Example 1, yielding an excellent correlation and revealing a high degree of confidence in the ability of the package to yield accurate dosimetry data for the contents packaged therein.

What is claimed is:

1. A dosimetric package comprising a product, a packaging material covering at least a portion of the product, and an integral dosimetric agent incorporated into the dosimetric package, wherein the integral dosimetric agent has a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis.

2. The dosimetric package of claim 1, wherein the integral dosimetric agent is incorporated in the product.

3. The dosimetric package of claim 1, wherein the integral dosimetric agent is incorporated in the packaging material.

4. The dosimetric package of claim 1, wherein the second, activated state of the integral dosimetric agent is detectable by electron spin resonance spectroscopy.

5. The dosimetric package of claim 4, wherein the second, activated state of the integral dosimetric agent is a free radical state.

6. The dosimetric package of claim 5, wherein the integral dosimetric agent comprises at least one of an amino acid, a sugar, and an amine salt of an organic acid.

7. The dosimetric package of claim 6, wherein the integral dosimetric agent comprises alanine.

8. The dosimetric package of claim 1, wherein the product comprises a medical device.

9. A method of making a dosimetric package comprising:

providing an integral dosimetric agent wherein the integral dosimetric agent has a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis;

incorporating the integral dosimetric agent into either or both of a product or a packaging material; and

packaging the product in the packaging material.

10. The method of claim 9, wherein the integral dosimetric agent is incorporated in the product.

11. The method of claim 9, wherein the integral dosimetric agent is incorporated in the packaging material.

12. The method of claim 9, wherein the second, activated state of the integral dosimetric agent is detectable by electron spin resonance spectroscopy.

13. The method of claim 12, wherein the second, activated state of the integral dosimetric agent is a free radical state.

14. The method of claim 13, wherein the integral dosimetric agent comprises alanine.

15. A method of characterizing a dosimetric package comprising:

providing a dosimetric package comprising a product, a packaging material covering at least a portion of the product, and an integral dosimetric agent incorporated in the dosimetric package, wherein the integral dosimetric agent has a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis;

subjecting the dosimetric package to spectroscopic analysis under conditions effective to produce the second, distinguishable spectroscopic response;

measuring the second, distinguishable spectroscopic response;

providing a correlation between a desired characteristic of the one or more packaging materials and/or the one or more products and the measured second, distinguishable spectroscopic response; and

utilizing information comprising the correlation and the measured second, distinguishable spectroscopic response to characterize the dosimetric package.

16. The method of claim 15, wherein the second, activated state of the integral dosimetric agent is a free radical state.

17. The method of claim 15, further comprising, prior to the step of subjecting the dosimetric package to spectroscopic analysis, subjecting the dosimetric package to a treatment effective to cause at least a portion the integral dosimetric agent to be activated to the second, activated state.

18. The method of claim 17, wherein the dosimetric package is subjected to a treatment comprising at least one of gamma radiation, electron beam radiation, corona discharge, plasma discharge, X-rays, and microwave energy.

19. The method of claim 15, wherein the spectroscopic analysis comprises analysis by electron spin resonance spectroscopy.

20. A method of quantifying an amount of ionizing radiation received by a dosimetric package, comprising:

providing a dosimetric package comprising a product, a packaging material covering at least a portion of the product and an integral dosimetric agent incorporated in the dosimetric package, wherein the integral dosimetric agent has a first, latent state that provides a first response to spectroscopic analysis and a second, activated state that provides a second, distinguishable response to spectroscopic analysis, comprising:

subjecting the dosimetric package to spectroscopic analysis under conditions effective to produce the second, distinguishable spectroscopic response; optionally after subjecting the dosimetric package to an amount of ionizing radiation effective to cause at least a portion the integral dosimetric agent to be activated to the second, activated state;

measuring the second, distinguishable spectroscopic response;

providing a correlation between the amount of ionizing radiation received by the dosimetric package and the measured second, distinguishable spectroscopic response; and

utilizing information comprising the correlation and the measured second, distinguishable spectroscopic response to determine the amount of ionizing irradiation received by the dosimetric package.

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(54) Title: DOSIMETRIC PACKAGE AND METHODS OF MAKING AND CHARACTERIZING SAME

(57) Abstract: The present invention provides a dosimetric package, a method of making the dosimetric package, and a method of characterizing a dosimetric package. The dosimetric package includes one or more products, one or more packaging materials covering at least a portion of the one or more products, as well as one or more integral dosimetric agents incorporated into the dosimetric package, such that the package itself possesses properties detectable by dosimetric analysis. The dosimetric package of the present invention may be dosimetrically analyzed, the result of which may be utilized to further determine characteristics of the dosimetric package such as, amount of ionizing radiation received by the dosimetric package, relative sterility, relative freshness, and the like.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/04712

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01T1/04 A61L2/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01T A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 501 945 A (KANAKKANATT SEBASTIAN V) 26 March 1996 (1996-03-26) column 2, line 10 - line 20; claim 1	1-20
X	US 3 899 677 A (HORI YUTAKA ET AL) 12 August 1975 (1975-08-12) column 2; claim 1	1-20
A	US 5 206 118 A (LYNCH DOREEN C ET AL) 27 April 1993 (1993-04-27) column 1-4; figure 1	1-20
A	WO 98 06574 A (GRACE W R & CO) 19 February 1998 (1998-02-19) claim 1; figure 1	1-20

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 October 2000	09/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mason, W

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/04712

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	GB 835 120 A (TI GROUP SERVICES) 18 May 1960 (1960-05-18) claim 1	1-20
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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